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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/957,709	10/24/1997	HOLLY HOGREFE	1486/41363CP	2438

7590 04/05/2007
FINNEGAN, HENDERSON, FARABOW, GARRETT
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WASHINGTON, DC 20005

EXAMINER

RAMIREZ, DELIA M

ART UNIT	PAPER NUMBER
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1652

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No. 08/957,709	Applicant(s) HOGREFE ET AL.	
	Examiner Delia M. Ramirez	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 December 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 17,46,59-66,77-79,87-89 and 95 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 17,46,59-66,77-79,87-89 and 95 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>12/26/06</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Status of the Application

Claims 17, 46, 59-66, 77-79, 87-89, 95 are pending.

Applicant's amendment of claim 17 as submitted in a communication filed on 12/26/2006 is acknowledged.

Applicant has indicated that papers submitted on 10/27/2006 with an IDS in copending application 09/631613 were mistakenly filed in the present application. Thus, these papers should not be considered as a response to the outstanding action. Applicant also requests removal of these documents from the file.

Upon review of the records of the instant application and copending application 09/631,613, the Examiner has been able to determine that the papers filed on 10/27/2006 are not a response to the Office action mailed on 8/24/2006. Specifically, the transmittal letter, claims and remarks dated 10/27/2006 are identical to those submitted on 6/9/2006 in the instant application. Thus, the Examiner has not considered these papers as a response to the outstanding action of 8/24/2006.

Claims 17, 46, 59-66, 77-79, 87-89, 95 are at issue and are being examined herein.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Information Disclosure Statement

1. The information disclosure statement (IDS) submitted on 12/26/2006 is acknowledged. The references have been considered by the Examiner. However, the amendment and response filed in 09/631613 cited herein are not true publications with a corresponding publication date. They are not fully in compliance with 37 CFR 1.97 and will not be printed on the face of a patent issuing from this application.

Claim Rejections - 35 USC § 112, First Paragraph

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
3. Claim 17 was rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. This rejection has been discussed at length in the Non Final Office action mailed on 8/24/2006.
4. In view of Applicant's amendment of the claim which now requires the *P. furiosus* protein to have nucleic acid polymerase enhancing activity, this rejection is hereby withdrawn.
5. Claims 17 and 95 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a protein complex comprising the polypeptide encoded by the polynucleotide of SEQ ID NO: 70, does not reasonably provide enablement for a protein complex comprising a polypeptide having polymerase enhancing activity encoded by a polynucleotide which hybridizes under the specific conditions recited to the complete complement of the polynucleotide of SEQ ID NO: 70. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.
6. Applicant traverses the rejection on the grounds that (1) the Examiner seeks to characterize proteins encoded by polynucleotides nearly 90% sequence identical to SEQ ID NO: 70 as proteins with low structural similarity, (2) the conditions recited in Example 9 of the USPTO Written Description Guidelines and those recited in the instant claims are stringent hybridization conditions, (3) the specification provides extensive guidance on the mechanism by which PEF can enhance an amplification reaction, (4) the specification provides an alignment of related proteins which shows conserved and non-conserved regions, (5) a considerable amount of experimentation is permissible, if it is merely routine, (6)

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the specification provides guidance as to which variants are more likely to have the recited activity, and

(7) the specification provides assays to screen for polypeptides having the recited activity.

7. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the instant rejection. The Examiner acknowledges the teachings of the specification and Example 9 of the Written Description Guidelines. The Examiner also agrees that a considerable amount of experimentation is permissible, if it is merely routine. However, the Examiner respectfully disagrees with Applicant's contention that the claimed invention is fully enabled by the teachings of the specification and/or the prior art.

With regard to Example 9, it is noted that this example is in regard to written description and not enablement. Thus, in accordance with the Written Description Guidelines, the Examiner is not rejecting the instant claims for lack of adequate written description.

The Examiner is not contending that all the nucleic acids which would hybridize to the polynucleotide of SEQ ID NO: 70 under the conditions recited will encode proteins with low structural similarity to the polypeptide of SEQ ID NO: 71. Certainly, one of skill in the art would expect many of the species recited to encode proteins having high structural similarity to the polypeptide of SEQ ID NO: 71. However, as clearly stated in the previous Office action, the genus of nucleic acids can potentially encompass polynucleotides encoding proteins having low structural similarity to the polypeptide of SEQ ID NO: 71 that could have the recited activity (62% sequence identity to SEQ ID NO: 71). In view of the fact that neither the specification nor the art teach (1) the degree of structural variability among proteins having nucleic acid polymerase enhancing activity, and/or (2) a structure/function correlation that would allow one of skill in the art to envision the structure of variants having the desired activity, one of skill in the art cannot, based solely on structural homology, determine a priori which species will or will not encode a protein having the recited activity. There is no sequence identity threshold below which one of skill in the art would not expect a variant to display the recited activity. Thus, the total

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number of variants having low structural homology and the recited function is unknown and cannot be predicted with the information provided.

While it is agreed that an alignment of related proteins has been provided, and one of skill in the art can determine conserved and non-conserved regions from such alignment, there is no teaching or suggestion indicating (1) that all the conserved regions in that alignment are associated with the recited activity, or (2) which of those conserved regions are related to the recited activity. In addition, there is no teaching/suggestion as to how the recited activity would be affected with any number of modifications within the non-conserved regions. As extensively discussed in the previous Office action, the art clearly teaches the difficulties in predicting how even small structural changes can affect function. See the teachings of Branden et al., Witkowski et al., and Seffernick et al. As taught by Witkowski et al., even a single conservative amino acid substitution was enough to significantly alter enzymatic activity. Also, it is noted that in some situations, the identity of the proteins included in an alignment may affect the location/sequence of the conserved regions. Thus, what appears to be a conserved region when aligning a set of proteins having activity X may not be the same conserved region when aligning a different set of proteins having activity X. Contrary to applicant's assertions, a disclosure of assays that would detect a particular activity, an alignment of related proteins showing conserved/non-conserved regions, and a discussion of the mechanism by which PEF can enhance an amplification reaction is not sufficient to enable the entire scope of the claimed invention because this information still would not provide sufficient guidance as to those structural elements which are essential for the recited activity such that only those variants comprising those structural elements can be selected for testing. In the absence of such guidance, the skilled artisan is left with the task of testing an essentially infinite number of species. Therefore, one of skill in the art cannot reasonably conclude that the full scope of the claimed invention is enabled by the teachings of the specification and/or the prior art.

Double Patenting

8. Claims 17, 46, 59-66, 77-79, 87-89 and 95 remain rejected under the judicially created doctrine of double patenting over claims 1, 5-9, 13-20, 23-24, 26-34 and 40-41 of U.S. Patent No. 6,183,997. This rejection has been discussed at length in Paper No. 25, mailed on 2/27/2002.

9. Applicants have indicated that if the instant claims are found allowable, a terminal disclaimer will be filed. Since a terminal disclaimer has not yet been filed and no arguments have been presented pointing out disagreements with the Examiner's contentions, the double patenting rejection is maintained for the reasons of record.

Conclusion

10. No claim is in condition for allowance.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

12. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should

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you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.



Delia M. Ramirez, Ph.D.
Primary Patent Examiner
Art Unit 1652

DR

March 28, 2007